A computational approach using Cellular Potts Model for simulation of neural stem cells grown in PCL-Graphene scaffolds.

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Abstract:

In the last decade, new computational model environment that includes both discrete and continuous models is getting more attention.One of the most well-known hybrid approaches is Cellular Potts Model also known as the Glazier-Graner-Hogeweg model, a lattice-based, cellular level computational framework that accurately describes biological phenomena including stem cell differentiation, tumor growth, cell migration, angiogenesis, cell rearrangement and adhesion. In this study we use the Cellular Potts Model (CPM) to design a dynamic microenvironment for cellular organization and its functioning at a Nano-scale level. Particularly we focus on cellular level interactions of neural stem cells grown on a Poly(ε-caprolactone) (PCL)-graphene scaffolds which are proven to provide better protein and cell adhesion and eventually increase the biological responses of the cells. The interactions such as cell-cell, cell-extracellular matrix adhesion and cellular motility contribute to the system's energy given by a function known as Hamiltonian which manages the lattice rearrangement using the stochastic Monte Carlo's model by minimizing the energy.

Introduction:

Regeneration of the neural cells damaged by injury or degenerative diseases, is limited to either replacement or repair of the neural cells. In order to replace neural cells, 3-D scaffolds that mimic the natural extracellular microenvironment are being used. Particularly we use Poly(ε-caprolactone) (PCL)-graphene scaffolds which have shown better cell guidance and improved electrical interactions of the neural cells. In this study we aim to analyse how this cells behave and migrate from the scaffold by using a computational approach known as Cellular Potts Model (CPM). CPM also known as the Glazier-Graner-Hogeweg (GGH) model, is a lattice-based, cellular level computational framework that accurately describes biological phenomena including cell migration, cell rearrangement and adhesion. The total energy of the system is given by the Hamiltonian function.

$$H(t) = H_{Adhesion(t)} + H_{Constraint(t)} + H_{Force(t)}$$

$$H_{Adhesion} = \sum_{x,x' \epsilon \Omega_{x'}} J_{\tau(\sum_{(x)},\tau(\sum \sigma'(x'))}\ (t)$$

$$H_{Constraint(t)} = \sum_{\sum}^{\sigma} \sum_{i-constraint} \lambda_{\sum}^{\sigma i}(t)\ [a_{\sum\sigma}^{i}\ (t) - A_{\sum\sigma}^{i}\ (t)]^2$$

$$H_{Force(t)} = \sum_{x \in \sum}^{\sigma} \sum_{k-force} \mu_{\sum(x)}^{k}\ (t) F^{k}\ (t) \cdot r_x$$

Proposed method:

In this simulation, the scaffold is set to have a volumetric extension of 1cm^3.The unit of time in this approach is given by Monte Carlo Step (MCS) and it is set to correspond to 2 s of the real experimental time. In order to provide migration to the cells, it is important to set proper values to the average velocity and the displacement by taking in consideration the Persistence-Random-Walk (PRW) law.Cellular matrix adhesion is provided mainly by ligands such as integrin and by modulating cell-fiber adhesion parameter J_{C-F}, adhesion is provided. The migration-adhesion relationship is determined by the value we give to the parameter J_{C-F}.

$$p_\eta \approx \frac{<d_\eta^2\ (t)>}{2v_\eta^2\ (t)t}$$

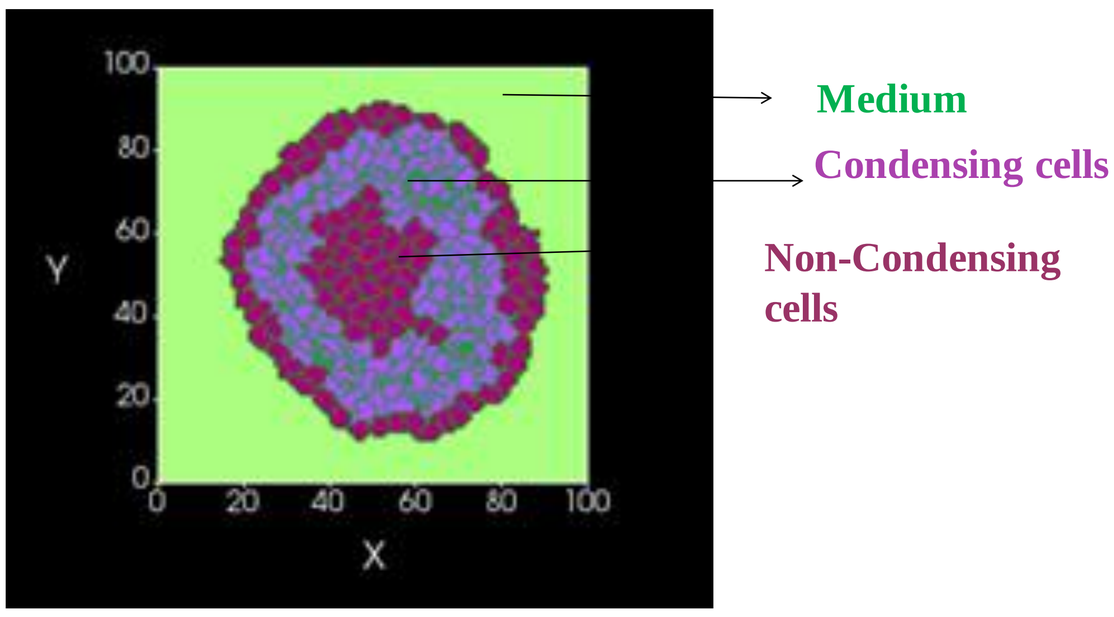

Fig1. Details of a typical two-dimensional (x-y) CPM configuration. Each coloured domain represents a single spatially-extended cell. The detail shows that each generalized cell is a set of cell-lattice sites (or pixel). Snapshot taken at 2500 MCS

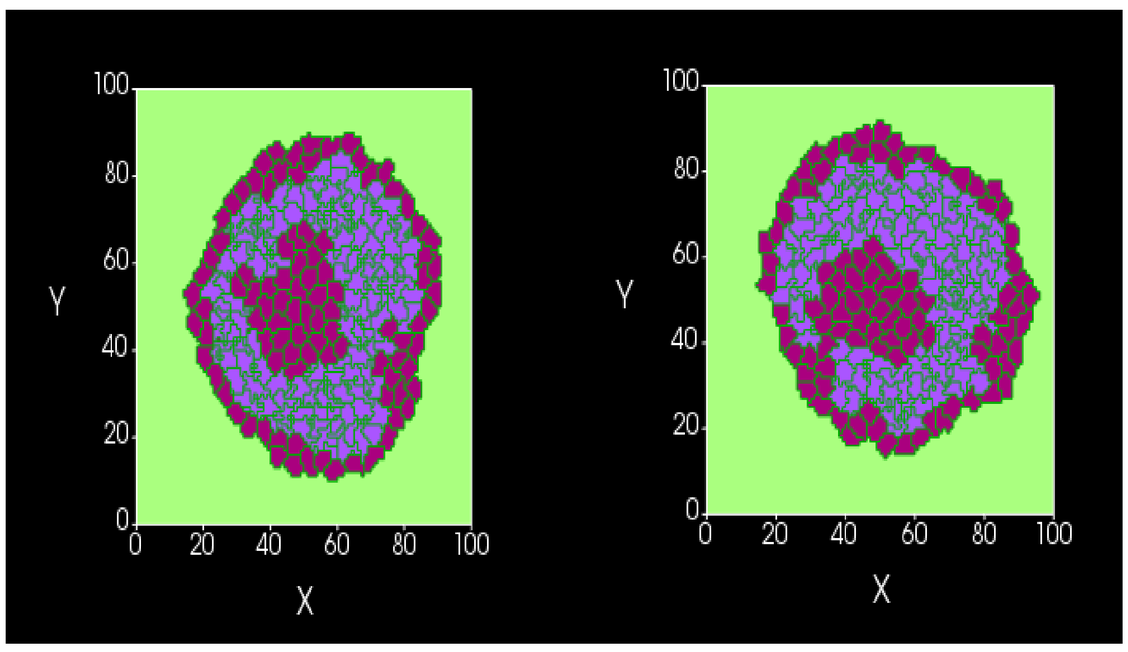

Fig2.a and fig2.b : The same simulation at different MCS ,4500 and 9900 MCS respectively. When comparing with the first figure ,we see that the cells are moving and distributed in different directions.

Parameter	Description
$A_C^{Surface}$	Surface of neural cells
$A_C^{Perimeter}$	Perimeter of neural cells
$\lambda_C^{Surface}$	Compressibility of neural cells
$\lambda_C^{Perimeter}$	Stiffness of neural cells
$J_{C,C}$	Cell-cell adhesion
$J_{C,M}$	Cell-matrix adhesion
T	Motility of the neural cells

Table1: Main parameters and their description

Conclusion and Discussion

Limitations of the CPM model are due to lack of mathematical methods available for deriving new laws that correspond to behaviours of different variables at cellular level. However ,the CPM model is used in various biological applications and in our study it is able to analyse the behaviour of the neural cells and their motility and migration from the scaffold.

References

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